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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,477	01/23/2002	F.C. Thomas Allnutt	031676.0208	9546

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EXAMINER	
CHEU, CHANGHWA J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,477	ALLNUTT ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *14-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-13, drawn to a method for detecting the presence or amount of docosahexaenoic acid (DHA) in a sample.

Group II, claim(s) 14-18, drawn to a kit for detecting DHA.

Group III, claim(s) 19-20, drawn to a recombinant fusion protein.

According to 37 CFR 1.475 regarding unity of invention:

(a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The inventions listed as Groups I and II do not relate to a single general inventive concept under 37 CFR 1.475 because, under 37 CFR 1.475, they lack the same or corresponding special technical features for the following reasons:

Xu et al. (J Biological Chem 1996 Vol. 271: 24711) teach using a brain lipid-binding protein (BLBP) to detect an essential fatty acid, i.e. docosahexaenoic acid (DHC), in the nervous

system. Xu et al. has show that the BLBP having differntial binding specificity for DHA over other fatty acids and can form complex with DHA. Therefore, the current invention does not contribute any special technical feature in light of Xu's reference. Accordingly, the instant invention, as a whole, lacks unity of inventive concept under 37 CFR 1.475.

2. During a telephone conversation with Mr. Posorske on August 6, 2004, a provisional election was made with traverse to prosecute the invention of group I, claim1-13. Affirmation of this election must be made by applicant in replying to this Office action. Claims 14-20 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

4. Claims 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5)

the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The current invention directs to a method of detecting the presence or amount of docosahexaenoic acid (DHA) in a sample by contacting a sample with a protein having specificity for DHA, and detecting the binding of the protein /DHA complex. Applicant recites in claims 12-13 including a step of hydrolyzing complex lipids to release DHA residues as free DHA. First, there is no specific agent(s) or working examples has been shown as to what kind of agents can be used to release, i.e. non-enzymatically, this DHA molecules from lipid complex. Applicant merely discusses in general using "detergent or lipid micelles" in fluorescence polarization assay (See page 20, last paragraph to page 21, first paragraph). However, applicant states that "detergent or lipid micelles *may be added to take up* the released fatty acid and/or label, thereby decreasing depolarization" (page 21, first paragraph)(emphasis added). Applicant asserts a hydrolyzing step, whereas the detergents or lipid micelles are generally not considered hydrolyzing agents. According to the specification, detergent or lipid micelles may be added to *take up* the released fatty acid (emphasis added). Their function is not to release DHA from complex lipids but to *take up* the DHA residues. It is not clear what causes the release of the DHA. Second, claims 12 recites using a hydrolyzing step in order to release DHA residues from complex lipids. It is unclear what agent, in particular, can release the instant recited fatty acid, i.e. DHA, from other fatty acids, such as oleic acid, aracidonic acid, or eicosanoic acid in a lipid complex because all of the fatty acids share common hydrophobic characteristic. In view of the aforementioned lack of predictability in the art, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in the applicant's specification of how to effectively practice the recited method and absent working examples.

Written Description

5. Claims 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed hydrolyzing agent(s) specific for DHA, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 9, "immobilized" is vague and indefinite. It is not clear where and how this protein is immobilized.

With respect to claim 12, line 2, "complex lipids" is vague and indefinite. It is not clear whether this complex is the same as the "DHA-protein complex" as recited in claim 1.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-2, 4-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al. (J Biological Chem (1996) 271: 24711).

Xu et al. disclose a method of detecting the DHA by using its recognizing protein, i.e. brain lipid-binding protein (BLBP). Xu et al. teach using a recombinant BLBP immobilized in a Lipidex 1000 column for fatty acid binding assay (See Methods and Materials). The BLBP has differential binding specificity for DHA over other fatty acids, such as oleic acid (OA), aracidonic acid (AA), or eicosanoic acid. In particular, DHA possesses higher affinity than those fatty acids. For instance, Xu et al. found out that there is a 20-fold increase in affinity of BLBP for DHA compared to OA or AA (See Table I for the Kd values; and page 24717, right column, third paragraph). Xu et al. label fatty acid, e.g. H^3, as a detecting means to measure the binding between the fatty acid and BLBP protein (See Figure 2 and 3 and Table 1).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al. in view of Ullman et al. (US 6326159).

Xu et al. reference has been discussed but is silent in using a protein, i.e. antibody to detect the DHA-BLBP complex. Ullman et al. review a method of producing an antibody recognizing a complex formed by a target ligand bound with ligand binding partner protein (Col. 5, line 30-45; Abstract; Example 8). Ullman et al. indicate that using a second antibody specifically for the complex of ligand with ligand protein can enhance specificity of binding results (See Col. 17, line 45-60). The technique of making the antibody involves routine skilled in the art. Supra. Therefore, it would have been obvious to one skilled in the art at the time the invention was made to have provided Xu et al. with the antibody specific for recognizing the complex of the BLBP and DHA for enhance specificity.

12. Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al..

Xu et al reference has been discussed but is silent in using biological samples in the analysis. However, Xu et al. review the role of BLBP in the developing central nervous system, including cell differentiation, signal transduction, and regulatory upregulation (See Introduction). Xu et al. also disclose the target ligand (DHA) for the BLBP in this prior art reference. It would have been obvious to one skilled in the art at the time when invention was made to apply the method of binding between BLBP and DHA in a biological sample with reasonable expectation of success because the target ligand DHA for BHA is known, and understanding the development processes is of great interest in research field, and biological sample preparation involves merely routine practice in the art.

Conclusion

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-282-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

August 10, 2004

BAO-THUY L. NGUYEN
PRIMARY EXAMINER
8/16/04

Notice of References Cited	Application/Control No. 09/937,477	Applicant(s)/Patent Under Reexamination ALLNUTT ET AL.	
	Examiner Jacob Cheu	Art Unit 1641	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-6,326,159	12-2001	Ullman et al.	435/7.7
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
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	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
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	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

FORM PTO-1449 (Modified) (REV. 7-80)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. 031676.0208	APPLICATION NO. 09/937,477
LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary)		APPLICANT Thomas F. C. ALLNUTT, et al.	
		FILING DATE September 26, 2001	GROUP To Be Assigned

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A	5 7 7 7 1 4 1	7/1998	Brunner, et al.			
	B	5 5 5 0 1 5 6	8/1996	Kyle			
	C	5 3 9 7 5 9 1	3/1995	Kyle, et al			
	D	4 9 4 3 5 2 7	7/1990	Protter, et al.			
	E	4 2 8 1 0 6 1	7/1981	Zuk, et al.			

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE		CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	F	WO 98 5 7 1 7 1	12/1998	PCT				
	G	WO 98 0 3 1 5 9	1/1998	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)

H	XU, L. et al.; "Ligand Specificity of Brain Lipid-binding Protein", The Journal of Biological Chemistry, *Vol.* 271, 24711-24719, (1996)
I	KUHAR, S., et al.; "Changing Patterns of gene expression define four stages of cerebellar granule neuron differentiation", Development, *Vol.* 117, 97-104, (1993)
J	KURTZ, A., et al.; "The expression pattern of a novel gene encoding brain-fatty acid binding protein correlates with neuronal and glial cell development, Development, *Vol.* 120, 2637-2649, (1994)
K	FENG, L., et al.; "Differentiating neurons activate transcription of the brain lipid-binding protein gene in radial glia through a novel regulatory element", Development, *Vol.* 121, 1719-1730, (1995)
L	FENG, L., et al.; "Brain Lipid-Binding Protein (BLBP): A Novel Signaling System in the Developing Mammalian CNS, Neuron, *Vol.* 12, 895-908, (1994)
M	SCHOENTGEN, F., et al.; "Amino acid sequence and some ligand binding properties of fatty acid-binding protein from bovine brain, Molecular and Cellular Biochemistry, *Vol.* 98, 35-39, (1990)
N	MYERS-PAYNE, S., et al.; "Isolation and Characterization of Two Fatty Acid Binding Proteins from Mouse Brain", Journal of Neurochemistry *Vol.* 66, 1648-1656, (1996)
O	ROUSSELOT, P., et al.; "Expression of Brain Lipid Binding Protein in the Brain of the Adult Canary and Its Implications for Adult Neurogenesis", The Journal of Comparative Neurology, *Vol.* 385, 415-426, (1997)
P	KAIKAUS, R., et al.; "Functions of fatty acid binding proteins", Experientia, *Vol.* 6, 617-630, (1990) Abstract only)

EXAMINER	DATE CONSIDERED 8/12/04

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